

What is claimed is:

1. A method for providing new therapeutic agent(s), characterized in that it comprises the following steps:
  - a) selecting at least one polypeptide encoded by a natural allelic variant of one preselected gene with therapeutic potential and/or of at least one related gene thereof;
  - b) determining the therapeutic index of the polypeptide(s) selected in step a); and
  - c) retaining as therapeutic agent(s), the polypeptide(s) selected in step a) whose therapeutic index, as determined in step b), is higher than a therapeutic index of reference.
2. The method according to claim 1, wherein the therapeutic index in step b) is determined without resorting to *in vivo* activity tests.
3. The method according to claim 1 or 2, characterized in that at least 2 polypeptides, preferably at least 4 polypeptides, are selected in step a).
4. The method according to any one of claims 1 to 3, wherein the therapeutic index of reference is the therapeutic index of one reference product.
5. The method according to any one of claims 1 to 4, characterized in that it further comprises a step d), wherein only the polypeptide(s) retained in step c) which has (have) the highest or second highest therapeutic index is (are) selected as therapeutic agent(s).
6. The method according to any one of claims 1 to 5, characterized in that step b) comprises the following steps:
  - i) submitting the polypeptides selected in step a) to at least two activity tests;
  - ii) attributing a value to each polypeptide in direct relation with the results of said activity tests; and
  - iii) determining the therapeutic index of each polypeptide from the values attributed in step ii).
7. The method according to any one of claims 3 to 6, wherein the polypeptides selected in step a) are:
  - polypeptides encoded by natural allelic variants of one preselected gene with therapeutic potential; and

- polypeptides encoded by natural allelic variants of at least one related gene.
8. The method according to any one of claims 1 to 7, wherein said natural allelic variants originate from the same species.
9. The method according to claim 8, wherein said natural allelic variants originate from the human species.
10. The method according to any one of claims 1 to 9, wherein the polypeptides selected in step a) are polypeptides encoded by natural allelic variants of one single gene that can be either the preselected gene with therapeutic potential or one related gene thereof.
11. The method according to any one of claims 1 to 10, wherein the polypeptides selected in step a) are under their mature form.
12. The method according to any one of claims 1 to 11, wherein the amino acid sequences of the mature form of all the polypeptides selected in step a) differ one from each other by less than 20 amino acids, preferably by less than 10 amino acids, more preferably by only one single amino acid.
13. The method according to any one of claims 1 to 12, wherein said preselected gene with therapeutic potential is a gene encoding a cytokine.
14. The method according to claim 6, wherein at least one activity test is carried out by means of a gene expression vector carrying a polynucleotide which encodes one of the polypeptides selected in step a).
15. A therapeutic agent obtainable by the method according to any one of claims 1 to 14, and which consists of a polypeptide.
16. A therapeutic agent comprising a polynucleotide encoding a polypeptide according to claim 15, a gene expression vector comprising said polynucleotide and/or a host cell comprising said gene expression vector.
17. A therapeutic agent characterized in that it comprises:
- (i) a derivative of a polynucleotide encoding a polypeptide as defined in claim 15, or
  - (ii) a derivative of a polypeptide as defined in claim 15, said polypeptide being modified in order to increase its therapeutic index, or
  - (iii) a combination of a derivative of a polypeptide under (ii) with a derivative of a polynucleotide under (i).

18. The therapeutic agent of claim 17 wherein said modification to said polypeptide is selected from the group consisting of PEGylation, glycosylation, and succinylation.
- 5 19. The therapeutic agent of claim 17 wherein said modification to said polynucleotide involves a method selected from the group consisting of site-directed mutagenesis and directed evolution technologies, and increases the therapeutic index of the polypeptide encoded thereby.
- 10 20. A therapeutic agent comprising a recombinant polypeptide whose amino acid sequence comprises several, preferably all the natural genetic variations characterizing the polypeptides obtainable by the method according to any one of claims 1 to 14.
21. The use of a therapeutically effective amount of a therapeutic agent according to any one of claims 15 to 20 for the manufacture of a medicine for the treatment of a patient in need thereof.
- 15 22. The use of the method according to any one of claims 1 to 14 to provide new therapeutic agents with new pharmacological profiles, and/or to provide new therapeutic agents for new therapeutic applications, with respect to a reference product.